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NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 FEB 27 New STN AnaVist pricing effective March 1, 2006  
NEWS 4 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records  
NEWS 5 MAY 11 KOREAPAT updates resume  
NEWS 6 MAY 19 Derwent World Patents Index to be reloaded and enhanced  
NEWS 7 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAPLUS and  
USPATFULL/USPAT2  
NEWS 8 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS  
NEWS 9 JUN 02 The first reclassification of IPC codes now complete in  
INPADOC  
NEWS 10 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and  
and display fields  
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL  
NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced  
NEWS 13 JUL 14 FSTA enhanced with Japanese patents  
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI  
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive  
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced  
NEWS 17 AUG 30 CA(SM)/CAPLUS(SM) Austrian patent law changes  
  
NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.  
  
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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:13:25 ON 08 SEP 2006

=> file medline

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.42

0.42

FILE 'MEDLINE' ENTERED AT 14:14:16 ON 08 SEP 2006

FILE LAST UPDATED: 7 Sep 2006 (20060907/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).

See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s taxol or paclitaxel
      4415 TAXOL
        9 TAXOLS
      4419 TAXOL
          (TAXOL OR TAXOLS)
      12511 PACLITAXEL
        2 PACLITAXELS
      12511 PACLITAXEL
          (PACLITAXEL OR PACLITAXELS)
L1      13605 TAXOL OR PACLITAXEL
```

```
=> s microtubule?
L2      35292 MICROTUBULE?
```

```
=> s l2 (l) fluorescen?
      320554 FLUORESCEN?
L3      1923 L2 (L) FLUORESCEN?
```

```
=> s l3 adn l1
MISSING OPERATOR L3 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.
```

```
=> s l3 and l1
L4      188 L3 AND L1
```

```
=> s screen? or identit?
      278311 SCREEN?
        72439 IDENTIT?
L5      347554 SCREEN? OR IDENTIT?
```

```
=> s l5 and l4
L6      13 L5 AND L4
```

```
=> s l6 not @py>2002
'2002' NOT A VALID FIELD CODE
      0 @PY>2002
L7      13 L6 NOT @PY>2002
```

=> s 16 not py>2002  
2247673 PY>2002  
(PY>20029999)  
L8 5 L6 NOT PY>2002

=> d ibib abs 1-5

L8 ANSWER 1 OF 5 MEDLINE on STN  
ACCESSION NUMBER: 2003010607 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12516963  
TITLE: Synthesis and high content cell-based profiling of simplified analogues of the microtubule stabilizer (+)-discodermolide.  
AUTHOR: Minguez Jose M; Giuliano Kenneth A; Balachandran Raghavan; Madiraju Charitha; Curran Dennis P; Day Billy W  
CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, USA.  
CONTRACT NUMBER: CA78039 (NCI)  
SOURCE: Molecular cancer therapeutics, (2002 Dec) Vol. 1, No. 14, pp. 1305-13.  
Journal code: 101132535. ISSN: 1535-7163.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200306  
ENTRY DATE: Entered STN: 9 Jan 2003  
Last Updated on STN: 19 Jun 2003  
Entered Medline: 18 Jun 2003  
AB (+)-Discodermolide, a C24:4, trihydroxylated, octamethyl, carbamate-bearing fatty acid lactone originally isolated from a Caribbean sponge, has proven to be the most potent of the microtubule-stabilizing agents. Recent studies suggest that it or its analogues may have advantages over other classes of microtubule-stabilizing agents. (+)-Discodermolide's complex molecular architecture has made structure-activity relationship analysis in this class of compounds a formidable task. The goal of this study was to prepare simplified analogues of (+)-discodermolide and to analyze their biological activities to expand structure-activity relationships. A small library of analogues was prepared wherein the (+)-discodermolide methyl groups at C-14 and C-16 and the C-7 hydroxyl were removed, and the lactone was replaced by simple esters. The library components were analyzed for microtubule-stabilizing actions in vitro, antiproliferative activity against a small panel of human carcinoma cells, and cell signaling, microtubule architecture and mitotic spindle alterations by a multiparameter fluorescence cell-based screening technique. The results show that even drastic structural simplification can lead to analogues with actions related to microtubule targeting and signal transduction, but that these subtle effects were illuminated only through the high information content cell-based screen.  
  
L8 ANSWER 2 OF 5 MEDLINE on STN  
ACCESSION NUMBER: 2002009740 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11347885  
TITLE: Determination of the net exchange rate of tubulin dimer in steady-state microtubules by fluorescence correlation spectroscopy.  
AUTHOR: Neumann T; Kirschstein S O; Camacho Gomez J A; Kittler L; Unger E  
CORPORATE SOURCE: Institut fur Molekulare Biotechnologie e. V. Jena, Germany.  
SOURCE: Biological chemistry, (2001 Mar) Vol. 382, No. 3, pp. 387-91.  
Journal code: 9700112. ISSN: 1431-6730.

PUB. COUNTRY: Germany; Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 21 Jan 2002  
Last Updated on STN: 21 Jan 2002  
Entered Medline: 4 Dec 2001

AB The microtubule cytoskeleton plays an important role in eukaryotic cells, e. g., in cell movement or morphogenesis. Microtubules, formed by assembly of tubulin dimers, are dynamic polymers changing randomly between periods of growing and shortening, a property known as dynamic instability. Another process characterizing the dynamic behaviour is the so-called treadmilling due to different binding constants of tubulin at both microtubule ends. In this study, we used tetramethylrhodamine (TMR)-labeled tubulin added to microtubule suspensions to determine the net exchange rate (NER) of tubulin dimers by fluorescence correlation spectroscopy (FCS) as a measure for microtubule dynamics. This approach, which seems to be suitable as a screening system to detect compounds influencing the NER of tubulin dimers into microtubules at steady-state, showed that taxol, nocodazole, colchicine, and vinblastine affect microtubule dynamics at concentrations as low as  $10(-9)$ - $10(-10)$  M.

L8 ANSWER 3 OF 5 MEDLINE on STN  
ACCESSION NUMBER: 2001563701 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11668581  
TITLE: Abundant expression of the microtubule-associated protein, ensconsin (E-MAP-115), alters the cellular response to Taxol.  
AUTHOR: Gruber D; Faire K; Bulinski J C  
CORPORATE SOURCE: Department of Biological Sciences, Columbia University, New York, New York 10027, USA.  
CONTRACT NUMBER: AR 08316 (NIAMS)  
CA 70951 (NCI)  
SOURCE: Cell motility and the cytoskeleton, (2001 Jul) Vol. 49, No. 3, pp. 115-29.  
Journal code: 8605339. ISSN: 0886-1544.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200201  
ENTRY DATE: Entered STN: 23 Oct 2001  
Last Updated on STN: 25 Jan 2002  
Entered Medline: 10 Jan 2002

AB Correlation between expression level of a microtubule-associated protein called ensconsin (E-MAP-115) and degree of Taxol sensitivity in several cultured cell lines prompted us to investigate potential cause-and-effect relationships between ensconsin level and Taxol action. We used human MCF-7 or HeLa cells, which are sensitive to low Taxol concentrations (LD(50) of 30-35 and 3.5 nM, respectively) to prepare stably transfected populations of cells expressing heterogeneous levels of ensconsin chimeras, either green fluorescent protein (GFP) conjugated to full-length ensconsin (GFP-Ens) or to ensconsin's microtubule-binding domain (GFP-EMTB). Both a subjective microscopic assay, i.e., scoring fluorescence of GFP-ensconsin chimeras following Taxol treatment, and a quantitative immunobiochemical assay, i.e., measuring level of GFP-ensconsin chimera in cells surviving treatment with Taxol, showed that cells expressing higher levels of GFP-ensconsin chimera were killed more readily by Taxol concentrations

approaching the LD(50). In contrast, in TC-7 cells, which are relatively insensitive to Taxol (LD(50) > 600 nM), high-level expression of GFP-EMTB conferred no significant susceptibility to killing by Taxol. However, heightening the Taxol sensitivity of GFP-EMTB-TC-7 cells by pre-incubating cells with the p-glycoprotein inhibitor, verapamil, did result in selective killing of cells highly expressing GFP-EMTB. Taken together, results obtained in MCF-7, HeLa, and TC-7 cells suggest that elevated ensconsin level bestowed a selective disadvantage upon Taxol-sensitive cells. To probe potential mechanisms by which ensconsin could alter the Taxol response, we isolated microtubules from HeLa cells that were or were not pretreated with Taxol. In vivo Taxol treatment significantly tightened microtubule-binding of ensconsin, suggesting that Taxol alters ensconsin's microtubule-binding properties and may, in turn, alter the Taxol response of the microtubules. Our data support the hypothesis that Taxol works synergistically or in concert with microtubule-binding proteins in bringing about deleterious effects on the microtubule cytoskeleton.

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L8 ANSWER 4 OF 5 MEDLINE on STN  
 ACCESSION NUMBER: 2001070643 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11000580  
 TITLE: Cross-resistance in the 2',2'-difluorodeoxycytidine (gemcitabine)-resistant human ovarian cancer cell line AG6000 to standard and investigational drugs.  
 AUTHOR: Bergman A M; Giaccone G; van Moorsel C J; Mauritz R; Noordhuis P; Pinedo H M; Peters G J  
 CORPORATE SOURCE: Department of Medical Oncology, University Hospital Vrije Universit., PO Box 7057, 1007 MB Amsterdam, The Netherlands.  
 SOURCE: European journal of cancer (Oxford, England : 1990), (2000 Oct) Vol. 36, No. 15, pp. 1974-83.  
 Journal code: 9005373. ISSN: 0959-8049.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200101  
 ENTRY DATE: Entered STN: 22 Mar 2001  
 Last Updated on STN: 22 Mar 2001  
 Entered Medline: 4 Jan 2001

AB Gemcitabine (2'-2'-difluorodeoxycytidine; dFdC) is a deoxycytidine analogue which is effective against solid tumours, including lung cancer and ovarian cancer. dFdC requires phosphorylation by deoxycytidine kinase (dCK) for activation. In the human ovarian cancer cell line A2780 and its 30,000-fold dFdC-resistant variant AG6000 (P<0.001), we investigated the cross-resistance profile to several drugs. AG6000, which has a complete dCK deficiency, was approximately 1000-10,000-fold resistant to other deoxynucleoside analogues such as 1-beta-D-arabinofuranosyl cytosine, 2-chloro-deoxyadenosine, aza-deoxycytidine and 2', 2'-difluorodeoxyguanosine (dFdG) (P<0.001). dFdG can be activated by dCK and deoxyguanosine kinase (dGK), but the latter enzyme was not altered in AG6000 cells. Thus dFdG resistance was only due to dCK deficiency. AG6000 was 1.6- and 46.7-fold resistant to 5-fluorouracil (5-FU) and ZD1694, respectively (the latter was significant; P<0.01), which may be due to the 1.7-fold higher thymidylate synthase (TS) activity, but AG6000 cells were also 2.7-fold resistant to the lipophilic TS inhibitor AG337 (P<0.05). Remarkably, AG6000 cells were 2.5-fold more sensitive to methotrexate (MTX) (P<0.01) than A2780 cells, but 1.6-fold more resistant to trimetrexate (TMQ) (P<0.10). However, no differences in reduced folate carrier activity, folylpolyglutamate synthetase (FPGS) activity and

polyglutamation of MTX were found between the cell lines. AG6000 cells were approximately 2 to 7.5-fold more resistant to doxorubicin (DOX), daunorubicin (DAU), epirubicin and vincristine (VCR) (the latter was significant;  $P < 0.02$ ) and approximately 4-fold more resistant to the microtubule inhibitors paclitaxel and docetaxel ( $P < 0.001$ ). Fluorescent activated cell sorter (FACS) analysis revealed no P-glycoprotein (Pgp) or multidrug resistance-associated protein (MRP) expression, but less fluorescence of intercalated DAU in AG6000 cells. An approximately 2-fold resistance to the topoisomerase I and II inhibitors etoposide, CPT-11 and SN38 was found in AG6000 cells. Topoisomerase I and II $\alpha$  RNA expression was decreased in AG6000 cells. AG6000 was 2.4, 2.4, 2.3 and 3.7-fold more resistant to EO9 ( $P < 0.02$ ), mitomycin-C (MMC) ( $P < 0.05$ ), cisplatin (CDDP) ( $P < 0.10$ ) and maphosphamide (MAPH), respectively. DT-diaphorase (DTD), which activates EO9, was 2.2-fold lower in AG6000 cells. CDDP resistance might be related to a reduced retention of DNA adducts in AG6000. However, glutathione levels were equal in A2780 and AG6000 cells. A 24 h exposure to DOX, VCR and paclitaxel at equimolar and equitoxic concentrations, resulted in more double-strand breaks (1.5- to 2-fold) in A2780 than in AG6000 cells. MAPH at 1120 nM and 17 nM of EO9 did not cause DNA damage in either cell line. In conclusion, AG6000 is a cell line highly cross-resistant to a wide variety of drugs. This cross-resistance might be related to altered enzyme activities and/or increased DNA repair.

L8 ANSWER 5 OF 5 MEDLINE on STN  
 ACCESSION NUMBER: 93355288 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8102497  
 TITLE: Localization of an exchangeable GTP binding site at the plus end of microtubules.  
 AUTHOR: Mitchison T J  
 CORPORATE SOURCE: Department of Pharmacology, University of California, San Francisco 94143-0450.  
 CONTRACT NUMBER: GM-39565 (NIGMS)  
 SOURCE: Science, (1993 Aug 20) Vol. 261, No. 5124, pp. 1044-7.  
 Journal code: 0404511. ISSN: 0036-8075.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199309  
 ENTRY DATE: Entered STN: 1 Oct 1993  
 Last Updated on STN: 3 Feb 1997  
 Entered Medline: 14 Sep 1993

AB Microtubule polarity arises from the head-to-tail orientation of alpha-beta tubulin heterodimers in the microtubule lattice. The identity of the polypeptide at each end of the microtubule is unknown, but structural models predict that the beta-tubulin end contains an exchangeable guanosine triphosphate (GTP) binding site. When GTP-coated fluorescent beads were incubated with microtubules, they bound specifically to plus ends, suggesting that tubulin is oriented in microtubules with beta-tubulin toward the plus end.

=> d kwic 2

L8 ANSWER 2 OF 5 MEDLINE on STN  
 TI Determination of the net exchange rate of tubulin dimer in steady-state microtubules by fluorescence correlation spectroscopy.  
 AB The microtubule cytoskeleton plays an important role in eukaryotic cells, e. g., in cell movement or morphogenesis. Microtubules, formed by assembly of tubulin dimers, are dynamic polymers changing randomly between periods of growing and shortening, a

property known. . . instability. Another process characterizing the dynamic behaviour is the so-called treadmilling due to different binding constants of tubulin at both microtubule ends. In this study, we used tetramethylrhodamine (TMR)-labeled tubulin added to microtubule suspensions to determine the net exchange rate (NER) of tubulin dimers by fluorescence correlation spectroscopy (FCS) as a measure for microtubule dynamics. This approach, which seems to be suitable as a screening system to detect compounds influencing the NER of tubulin dimers into microtubules at steady-state, showed that taxol, nocodazole, colchicine, and vinblastine affect microtubule dynamics at concentrations as low as  $10(-9)$ - $10(-10)$  M.

CT . . . Fluorescent Dyes: CH, chemistry

Microtubules: CH, chemistry

Microtubules: DE, drug effects

\*Microtubules: ME, metabolism

Nocodazole: ME, metabolism

Nocodazole: PD, pharmacology

Paclitaxel: ME, metabolism

Paclitaxel: PD, pharmacology

Research Support, Non-U.S. Gov't

Rhodamines: CH, chemistry

\*Spectrometry, Fluorescence: MT, methods

Tubulin: CH, chemistry

Tubulin: DE, drug. . .

RN 31430-18-9 (Nocodazole); 33069-62-4 (Paclitaxel); 57-22-7

(Vincristine); 62669-72-1 (tetramethylrhodamine); 64-86-8 (Colchicine)

## WEST Search History





DATE: Friday, September 08, 2006

<b>Hide?</b>	<b>Set Name</b>	<b>Query</b>	<b>Hit Count</b>
	<i>DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L16	L15 and anisotrop\$	2
<input type="checkbox"/>	L15	L14 and l7	82
<input type="checkbox"/>	L14	l4 and (microtubul\$ and fluores\$)	98
<input type="checkbox"/>	L13	L11 and (microtubule\$ and fluoresen\$)	0
<input type="checkbox"/>	L12	L11 and (microtublule\$ and fluoresen\$)	0
<input type="checkbox"/>	L11	l9 and l4	18
<input type="checkbox"/>	L10	l9 an dl4	0
<input type="checkbox"/>	L9	l7.clm.	390370
<input type="checkbox"/>	L8	L7 and l4	409
<input type="checkbox"/>	L7	screen\$ or identif\$	1679804
<input type="checkbox"/>	L6	L5 and l2	8
<input type="checkbox"/>	L5	flutax\$	8
<input type="checkbox"/>	L4	l2.ab.	1044
<input type="checkbox"/>	L3	l1 and L2	4
<input type="checkbox"/>	L2	taxol or paclitaxel	17485
<input type="checkbox"/>	L1	(morales or pereira or blasco).in.	2392

END OF SEARCH HISTORY